

BIOGRAPHICAL SKETCH

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NAME: **Henry Hess**

eRA COMMONS USER NAME (credential, e.g., agency login): HENRYHESS

POSITION TITLE: Professor of Biomedical Engineering

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Technical University Clausthal-Zellerfeld, Germany	Prediploma	02/1993	Physics
Technical University Berlin, Germany	Diploma (M.Sc.)	04/1996	Physics
Free University Berlin, Germany	Dr. rer. nat. (Ph.D.)	12/1999	Physics
University of Washington, Seattle, WA	Postdoc	02/2002	Bioengineering

A. Personal Statement

During my M.S. and Ph.D. studies I specialized in optics, which led to a Ph.D. thesis in femtosecond laser spectroscopy and mass spectrometry. However, since my postdoctoral studies I have focused mainly on the construction of hybrid nanodevices integrating kinesin motor proteins as active components (a). The observation of these devices primarily relies on fluorescence microscopy techniques and has benefitted tremendously from the super-resolution concepts developed in recent years (b).

In the past 4 years we have pursued a new challenge: The directed transport of analyte molecules by affinity gradients on a surface or in a film (c). This has led us to acquire the experimental tools necessary for single molecule fluorescence microscopy and to develop analysis tools to interpret these images. For example, our “Fluorescent Single Molecule Imaging Analysis (FSMIA)” package designed to identify and characterize individual fluorescent spots in a stack of images is available for download at GitHub, and a new fitting algorithm has been explored in (d). We are currently completing the project and are preparing several manuscripts related to surface adsorption and diffusion of fluorescently labeled proteins and DNA strands.

The proposed project will allow us to bring our accumulated expertise in single molecule analysis to bear on a new challenge, offering my engineering students and me interesting experimental, computational, and statistical problems to work on. Milan Stojanovic, Sergei Rudchenko and I have been in conversations for almost a decade, but this project integrates our respective expertise and capabilities in a unique fashion. My group and I are fully committed to making this project a success.

- (a) **H. Hess***: “Engineering applications of biomolecular motors”, Annual Review of Biomedical Engineering, 13, 429-450 (2011). 89 citations (Google Scholar, October 2, 2018)
- (b) X. Zhao, H. Palacci, V. Yadav, M.M. Spiering, M.K. Gilson, P.J. Butler, **H. Hess***, S.J. Benkovic*, A. Sen*: “Substrate-driven chemotactic assembly in an enzyme cascade”, Nature Chemistry 10, 311-317 (2018). 8 citations (Google Scholar, October 2, 2018)

- (c) A. Sitt and **H. Hess***: “Active transport by surface chemical potential gradients for enhancing analyte collection in nanoscale sensors”, *Nano Letters*, 15(5), 3341-3350 (2015). 15 citations (Google Scholar, October 2, 2018)
- (d) S. He, **H. Hess***: “Fast single molecule localizations by pattern matching”, *Proc. SPIE 9721, Nanoscale Imaging, Sensing, and Actuation for Biomedical Applications XIII*, 97210X (March 7, 2016); doi:10.1117/12.2213166

B. Positions and Honors

Positions:

2000 – 2002	Postdoctoral Associate, Department of Bioengineering, University of Washington (Seattle, WA)
2002 – 2005	Research Assistant Professor, Department of Bioengineering, University of Washington, Seattle
2005 – 2009	Assistant Professor, Department of Materials Science and Engineering, University of Florida
2009 – 2013	Associate Professor, Department of Biomedical Engineering, Columbia University, New York
2013 – 2016	Associate Professor with tenure, Department of Biomedical Engineering, Columbia University
2016 – now	Professor with tenure, Department of Biomedical Engineering, Columbia University, New York

Honors:

1996	Erwin-Stephan-Award of the Technical University Berlin for outstanding graduates
2000	Wolfgang-Paul-Award of the German Society for Mass Spectrometry for best PhD thesis
2000	Feodor Lynen postdoctoral fellowship of the A. von Humboldt foundation (renewed 2001)
2007	Distinguished Mentor Award of the UF/HHMI “Science for Life” program
2007	NSF CAREER Award
2009	Invitation to the National Academy Keck Futures Initiative “Synthetic Biology”
2010	Invited Speaker, US National Academy of Engineering Frontiers of Engineering Meeting
2009 – 2013	Associate Editor, <i>Journal of Nanotechnology in Engineering and Medicine</i>
2010 – present	Member of Editorial Advisory Board, <i>Nano Letters</i>
2014 – present	Editor-in-Chief, <i>IEEE Transactions on NanoBioscience</i>

C. Contributions to Science

I. Molecular Shuttles powered by Kinesin Motor Proteins

Starting with my postdoctoral studies, a large part of my work was devoted to the engineering of hybrid nanodevices. Hybrid nanodevices aim to take advantage of biological components with superior or even unattainable performance relative to man-made components. In particular biomolecular motors exceed the performance of current synthetic molecular motors by orders of magnitude, but also other building blocks such as antibodies and enzymes can provide functions not attainable by synthetic components. At the core of our devices is typically a “molecular shuttle”, a nanoscale transport system which utilizes surface-adhered kinesin motor proteins to move microtubules functionalized with fluorophores for observation and linkers for cargo loading (1). Molecular shuttles are used in diverse applications such as surface imaging, force measurements, and biosensors (2), and enable the study of nanoscale engineering principles (3,4).

1. **H. Hess**, J. Clemmens, D. Qin, J. Howard, and V. Vogel*: “Light-Controlled Molecular Shuttles Made from Motor Proteins Carrying Cargo on Engineered Surfaces”, *Nano Letters*, 1 (5), 235-239 (2001). 346 citations (Google Scholar, October 2, 2018)
2. T. Fischer, A. Agarwal and **H. Hess***: “A smart dust biosensor powered by kinesin motors”, *Nature Nanotechnology*, 4, 162-166 (2009). 170 citations (Google Scholar, October 2, 2018)
3. E.L.P. Dumont, C. Do and **H. Hess***: “Molecular wear of microtubules propelled by surface-adhered kinesins”, *Nature Nanotechnology* 10, 166-169 (2015). 14 citations (Google Scholar, October 12, 2016)
4. **H. Hess***: “Engineering applications of biomolecular motors”, *Annual Review of Biomedical Engineering*, 13, 429-450 (2011). 81 citations (Google Scholar, October 19, 2017)

II. Active Self-Assembly Processes

While chemistry is very successful in creating molecules via chemical self-assembly, the ability of nature to hierarchically self-assemble proteins, cells, and tissues is unmatched. One of the obstacles is that chemical self-assembly relies on diffusion as a transport mechanism and on thermal forces to separate mismatched building blocks. Since diffusion rapidly slows as the building blocks grow in size, and thermal forces are soon dwarfed by the increasing interaction strength between larger building blocks, the size of the building blocks is limited. Molecular motors have the potential to enhance self-assembly processes (5), because they can tap into a reservoir of chemical energy to create large and sustained forces. Moreover, their directed and controllable force generation can enable control of the assembly process and lead to a variety of emergent phenomena. Our proof-of-principle demonstration (6) utilized “sticky” microtubules propelled by surface-adhered kinesin motors and showed that the interactions between these microtubules leads to the formation of extended wires and eventually small spools.

Supported by a NSF CAREER award, my research group has investigated this model system for active self-assembly both experimentally and theoretically. We were able to establish the mechanisms responsible for spool formation using a combination of experiments and computer simulations. Spool formation was found to originate from defects on the surface but also from the simultaneous joining of multiple microtubule bundles into a circular aggregate. By optimizing the parameters we obtained nearly millimeter-long wires. Our analytical models support the idea that active transport by molecular motors enables the assembly of significantly larger structures compared to self-assembly processes relying on diffusive transport (7,8).

5. **H. Hess***: “Self-assembly driven by biomolecular motors”, *Soft Matter*, 2, 669 – 677 (2006). 84 citations (Google Scholar, October 19, 2017)
6. **H. Hess***, J. Clemmens, C. Brunner, R. Doot, S. Luna, K.-H. Ernst and V. Vogel*: Molecular self-assembly of “Nanowires” and “Nanospools” using active transport”, *Nano Letters*, 5(4), 629-633 (2005). 147 citations (Google Scholar, October 19, 2017)
7. O. Idan, A.T. Lam, J. Kamcev, J. Gonzales, A. Agarwal, and **H. Hess***: “Nanoscale transport enables active self-assembly of millimeter-scale structures”, *Nano Letters*, 12, 240-245 (2012). 21 citations (Google Scholar, October 19, 2017)
8. A.T. Lam, V. VanDelinder, A.M.R. Kabir, **H. Hess***, G.D. Bachand* and A. Kakugo*: “Motor-driven active self-assembly”, *Soft Matter* 12(4), 988-997 (2016). 8 citations (Google Scholar, October 19, 2017)

III. Active Transport by Chemical Potential Gradients

We have demonstrated that biomolecular motors, such as kinesin, can be used to accelerate analyte capture in biosensors (c). However, their limited lifetime and fragility poses engineering challenges. We therefore investigated in collaboration with the research teams of J. Lahann (U. Michigan) and P. Braun (UIUC) if advanced polymeric coatings and gels can provide a binding energy gradient which actively moves analyte molecules towards target sites. A detailed model of the analyte transport and its dependence on the strength of interaction between analyte and matrix has been developed by us and the emerging phenomena have been described. We furthermore assisted with the analysis of an experimental demonstration of this unusual active transport process by the Braun group at UIUC. We believe that gradient-driven transport may be an underestimated contribution to intracellular transport.

9. A. Sitt and **H. Hess***: “Directed transport by surface chemical potential gradients for enhancing analyte collection in nanoscale sensors”, *Nano Letters*, 15(5), 3341-3350 (2015). 10 citations (Google Scholar, October 2, 2018)
10. C. Zhang‡, A. Sitt‡, H.-J. Koo, K.V. Waynant, **H. Hess***, B.D. Pate, P.V. Braun*: “Autonomic molecular transport by polymers containing programmed chemical potential gradients”, *JACS* 137(15), 5066-5073 (2015). 15 citations (Google Scholar, October 2, 2018)

IV. Enzyme Cascades on Nanoscale Scaffolds

The synthesis of biofuels and pharmaceuticals in bacterial cells can be enhanced by synthetic metabolic pathways. While much attention has been paid to the engineering of genetic circuits, the rational design of molecular factories has to accurately model the events at the protein level and the effects of spatial organization and different transport modes. In a series of publications (11,12,13,14) we elucidated the impact of spatial organization on the throughput of enzyme cascades. In collaboration with Jose Blanchet from the Department of

Industrial Engineering and Operations Research at Columbia University, we are working towards new approaches to model enzymatic reaction cascades on protein scaffolds.

11. O. Idan, **H. Hess***: "Origins of Activity Enhancement in Enzyme Cascades on Scaffolds", ACS Nano, 7, 8658-8665 (2013). 50 citations (Google Scholar, October 2, 2018)
12. Y. Zhang, S. Tsitkov, **H. Hess***: "Proximity Does Not Contribute to Activity Enhancement in the Glucose Oxidase-Horseradish Peroxidase Cascade", Nature Communications, 7,13982 (2016). 53 citations (Google Scholar, October 2, 2018)
13. Y. Zhang, **H. Hess***: "Toward rational design of high-efficiency enzyme cascades", ACS Catalysis, 7, 6018-6027 (2017). 21 citations (Google Scholar, October 2, 2018)
14. Y. Zhang, S. Tsitkov, **H. Hess***: "Complex dynamics in a two-enzyme reaction network with substrate competition", Nature Catalysis, 1, 276-281 (2018).

V. New Techniques for Nanoscale Measurements

Due to my background in experimental physics, and particularly in laser spectroscopy (15), I have broad theoretical knowledge and practical experience with optical measurements near their fundamental limits. Together with my collaborators I have made continuous technical contributions to the development and refinement of characterization techniques and measurement tools. This includes the integration of dual color imaging into a monochromator, the adaptation of fluorescence interference contrast (FLIC) microscopy to the imaging of nanostructures with nanometer precision (16,17), the measurement of the absolute brightness of fluorescent nanospheres, the application of Kalman filters to particle tracking, and the application of landing rate measurements to measure protein adsorption to non-fouling coatings.

Our recent efforts have focused on the study of surface mobility of individual proteins and DNA strands, utilizing the tools of single molecule microscopy. A successful instrumentation grant provided us in 2014 with a fully motorized epi-fluorescence microscope (Nikon Ti-E) with focus stabilization, the latest Total Internal Reflection illumination setup, and a back-illuminated CCD camera (Andor Ixon). Start-up funds are still available to improve this system. We have developed custom software to identify and fit the fluorescence signal of single molecules and plan to adapt this software package to the specific needs of this project. Finally, we are also exploring the use of novel algorithms to improve the accuracy and facility of image analysis (18, d).

15. **H. Hess**, K.R. Asmis, T. Leisner, and L. Wöste*: "Vibrational wave packet dynamics in the silver tetramer probed by charge-reversal femtosecond pump-probe spectroscopy", Eur. Phys. J. D, **16**, 145-149 (2001). 25 citations (Google Scholar, October 2, 2018)
16. J. Kerssemakers, J. Howard, **H. Hess**, S. Diez*: "The distance that kinesin holds its cargo from the microtubule surface measured by fluorescence-interference-contrast microscopy", PNAS 103, 15812-15817 (2006) 114 citations (Google Scholar, October 2, 2018)
17. X. Deng‡, S. He‡, F. Xie, C. Friedmann, **H. Hess,*** J. Lahann*: "Ultra-sensitive *in situ* fluorescence analysis using modulated fluorescence interference contrast at nanostructured surfaces", Advanced Materials 28(12), 2367-2373 (2016). 4 citations (Google Scholar, October 2, 2018)
18. S. He, X. Deng, J. Lahann, **H. Hess***: "A two-dimensional lock-in algorithm for signal analysis in patterned images", IEEE Transactions on Biomedical Engineering 63, 2436-2440 (2016). 1 citation (Google Scholar, October 2, 2018)

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing

1. National Science Foundation Hess H
Molecular-scale breaking due to repeated loading in nanomachines
ENG 1662329 9/1/17 – 8/31/2020
The effort funded by this grant studies degradation process in molecular machines.
2. Defense Threat Reduction Agency Hess H
Transport Processes on Enzyme Scaffolds
HDTRA 1-14-1-0515 7/22/2014-7/21/2019
The effort funded by this grant is focused on the study of enzyme cascades immobilized on scaffolds.

3. National Science Foundation Hess H
Creating Dynamic and Adaptive Force-Producing Nanostructures
 DMR 1807514 7/1/18 – 6/30/2021
 The effort funded by this grant aims to dynamically assemble motor proteins.
4. National Science Foundation Obermeyer A / Hess H
RoL: EAGER: DESYN-C3 Enzyme cascades in synthetic membraneless organelles
 ENG 1844149 9/1/18 – 8/31/2020
 The effort funded by this grant studies the kinetics of enzyme cascades in coacervate droplets.

Recently Completed (last three years)

5. YouV Labs, Inc. (subcontract from a National Science Foundation SBIR award) Hess H
Development of an accurate low-cost wearable UV dosimeter for the general population
 3/1/18 – 6/30/18
6. Army Research Office Hess H
Thermodynamics of Statistical Learning
 W911-NF-17-1-0107 2/13/2017-2/12/2018
 The effort aims to elucidate conceptual connections between statistical thermodynamics and machine learning.
7. Defense Threat Reduction Agency Hess H
Improving Sensing with Tethered Capture and Surface Diffusion
 HDTRA 1-12-1-0037 6/1/12 – 2/22/2017
 The work aimed to exploit surface mobility of weakly bound analytes for novel sensor designs.
8. Army Research Office Crutchfield JP
Information Engines: Nanoscale Control, Computing, and Communication Out of Equilibrium
 W911NF-13-1-0390 9/1/2013-12/31/2016
 The effort advanced non-equilibrium statistical thermodynamics. My group was responsible for experimental verification.
9. Army Research Office Hess H
Fluorescence microscope for the observation of biological nanomachines
 W911NF-14-1-0515 8/12014-7/31/2015
 This equipment grant allowed the purchase of a start-of-the-art fluorescence microscope with TIRF.